"Synopsis of proposed Ph.D. research work"

MULTI-COMPONANT DOMINO STRATEGIES FOR THE SYNTHESIS AND FUNCTIONALIZATION OF HETEROCYCLES

Submitted by

Susmita Mondal

Student ID: 03333091504

Registration No. - VB-1266 of 2013-14

Roll No. - Ph.D. (C.W.) Sik-Chem-36

Name of the Ph. D. Supervisor: Dr. Alakananda Hajra

Department of Chemistry
Visva-Bharati, Santiniketan
West Bengal

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Introduction:

Multicomponent reactions (MCRs) are defined as the reactions where more than two staring materials react to form a product, incorporating large portions of all the reactants. There are various classification schemes of MCRs are possible, *e.g*. according to the reaction mechanisms, the components involved or their elemental variability.[1] In addition, Green Chemistry highlights the development of environmentally benign chemical processes and technologies.[2] MCRs are convergent,[3] step- and atom-economy process and are capable with several greener features. These reactions are effective in building highly functionalized small organic molecules from commercially available starting materials in a single step with inherent flexibility for creating molecular complexity and diversity coupled with minimization of time, labour, cost and waste production.[4,5] Therefore, development of various multi-component reactions for the construction of heterocyclic motifs have attracted major interest from pharmaceutical groups.

The first multicomponent reaction (MCR) was reported by Strecker in 1850,[6] after that hundreds of MCRs have been described over the years. However, the discovery of novel MCRs is somewhat a topic of the past decade. With the appearance of high-throughput screening in the pharmaceutical industry over a decade ago, synthetic chemists were faced with the challenge of preparing large collections of molecules to satisfy the requirement for new compounds for screening. By virtue of its intrinsic high exploratory power, research on MCRs has naturally become a rapidly evolving field and since 1995 has attracted attention from both academic and industrial researchers. Therefore, it is not surprising that many efforts are currently being devoted to this new field of research.

The main objective of the present work is focused on MCRs where imidazo[1,2-*a*]pyridine is one of components and acts as carbon nucleophile.

Backgrounds of the work:

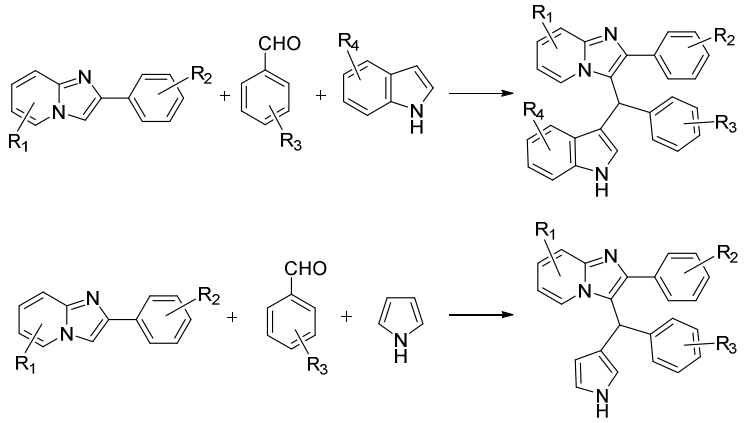
Imidazo[1,2-*a*]pyridines have evoked a large deal of interest because of their various biological properties.[7] Due to its wide applications in medicinal chemistry and pharmaceuticals, this fused bicyclic 5–6 heterocycle system is recognized as a privileged

drug scaffold. This scaffold is also important in the field of material science.[8] The pharmacological activity of imidazo[1,2-*a*]pyridine is shown to be dependent on the nature of substituents and functionalites at different positions. As a result, these 'privileged' fragments have become an intriguing area of synthetic interest and a number of efficient processes have been developed for the diversified synthesis of functionalized imidazo[1,2-*a*]pyridine derivatives.[9]

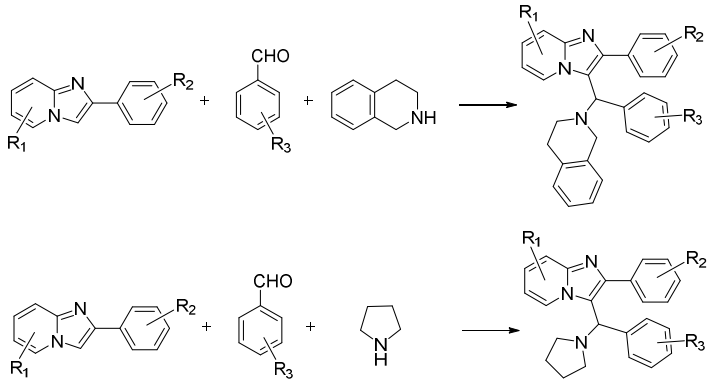
In continuation of our efforts to develop a number of synthetic techniques for the synthesis[10] and functionalization[11] of imidazo[1,2-*a*]pyridine derivatives employing readily available starting materials, we became interested in the construction of imidazo[1,2-*a*]pyridines attached with indole or pyrrole moieties because of the huge biological space of these compounds.

Work Plan:

Scheme 1:



Scheme 2:



Conclusion:

In summary, we want to develop novel MCR protocols for the construction of systems having imidazo[1,2-*a*]pyridine and indole/pyrrole moiety attached by a methylene group. These compounds may show high biological activities.

References:

1. J. Zhu and H. Bienayme, *In Multicomponent Reactions*; Eds.; Wiely-VCH Verlag GmbH & Co: KGaA, Weinheim, 2005 and references cited therein.
2. (*a*) P. T. Anastas and J. C. Warner, *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998; (*b*) P. T. Anastas and T. Williamson, *Green Chemistry, Frontiers in Benign Chemical Synthesis and Process*; Oxford University Press: Oxford, UK, 1998.
3. B. Beck, S. Hess and A. Do¨mling, *Bioorg. Med. Chem. Lett*., 2000, **10**, 1701.
4. (*a*) D. Tejedor and F. Garcia-Tellado, *Chem. Soc. Rev*., 2007, **36**, 484; (*b*) I. Ugi, *Pure Appl. Chem*. 2001, **73**, 187; For MCR-based heterocyclic libraries, see: (*c*) F. Lie'by-Muller, C. Simon, T. Constantieux and J. Rodriguez, *Qsar. Comb. Sci*., 2006, **25**, 432; (*d*) C. Simon, T. Constantieux and J. Rodriguez, *Eur. J. Org. Chem*., 2004, 4957; (*e*) N. M. Evdokimov, A. S. Kireev, A. A. Yakovenko, M. Y. Antipin, I. V. Magedov and A. Kornienko, *J. Org. Chem*., 2007, **72**, 3443; For drug discovery see: (*f*) L. Weber, *Drug Discovery Today,* 2002, **7***,* 143.
5. C. Hulme and V. Gore, Curr. *Med. Chem*., 2001, **10**, 51.
6. A. Strecker, *Liebigs Ann. Chem.,* 1850, **75**, 27.

7. (*a*) C. Enguehard-Gueiffier and A. Gueiffier, *Mini Rev. Med. Chem.*, 2007, **7**, 888; (*b*) A. T. Baviskar, S. M. Amrutkar, N. Trivedi, V. Chaudhary, A. Nayak, S. K. Guchhait, U. C. Banerjee, P. V. Bharatam and C. N. Kundu, *ACS Med. Chem. Lett*., 2015, **6**, 481.
8. (*a*) N. Shao, G.-X. Pang, C.-X. Yan, G.-F. Shi and Y. Cheng, *J. Org. Chem.,* 2011, **76**, 7458; (*b*) A. J. Stasyuk, M. Banasiewicz, M. K. Cyrański and D. T. Gryko, *J. Org. Chem.,* 2012, **77**, 5552.
9. (*a*) A. K. Bagdi, S. Santra, K. Monir and A. Hajra, *Chem. Commun.,* 2015, **51**, 1555; (*b*) K. Pericherla, P. Kaswan, K. Pandey and A. Kumar, *Synthesis,* 2015, **47**, 887; (*c*) J. Koubachi, S. E. Kazzouli, M. Bousmina and G. Guillaumet, *Eur. J. Org. Chem*., 2014, 5119; (*d*) H. Cao, X. Liu, L. Zhao, J. Cen, J. Lin, Q. Zhu and M. Fu, *Org. Lett.,* 2014, **16**, 146; (*e*) C. He, J. Hao, H. Xu, Y. Mo, H. Liu, J. Han and A. Lei, *Chem. Commun.,* 2012, **48**, 11073.
10. (*a*) S. Mishra, K. Monir, S. Mitra and A. Hajra, *Org. Lett.,* 2014, **16**, 6084; (*b*) K. Monir, A. K. Bagdi, M. Ghosh and A. Hajra, *Org. Lett.,* 2014, **16**, 4630; (*c*) A. K. Bagdi, M. Rahman, S. Santra, A. Majee and A. Hajra, *Adv. Synth. Catal.,* 2013, **355**, 1741.
11. (*a*) K. Monir, A. K. Bagdi, M. Ghosh and A. Hajra, *J. Org. Chem.,* 2015, **80,** 1332; (*b*) M. Ghosh, A. Naskar, S. Mitra and A. Hajra, *Eur. J. Org. Chem.,* 2015, 715; (*c*) A. K. Bagdi, S. Mitra, M. Ghosh and A. Hajra, *Org. Biomol. Chem*., 2015, **13**, 3314.